REMARKS

This Amendment and Reply seeks to place this application in condition for allowance. Certain claims have been amended to more clearly describe the invention, to more fully protect the invention, to improve grammar, to correct inadvertent typographical errors, and to address the Examiner's concerns regarding clarity. No new matter has been added.

All of the objections and rejections raised in the Office Action of April 7, 2005 (hereinafter the "Office Action") have been addressed. Each of the objections and rejections is addressed below in detail and in the order presented in the Office Action.

Objection to the Specification

The instant application has been amended to address the Examiner's concerns regarding use of trademarks. The trademarks are now presented in capitalized letters, as suggested by the Examiner (See, also, MPEP 608.01(v)). No new matter has been added.

Moreover, the use/presentation of such trademarks in the instant application is not intended to adversely affect the validity of the mark.

Objection to the Claims

In paragraph 3 of the Office Action, the Examiner expressed a concern that claims 2 and 3 are substantially duplicative of claims 4 and 5. Accordingly, claims 2 and 4 have been amended to address the Examiner's concern. No new matter has been added.

Claim Rejections – 35 USC §112

In paragraphs 4 and 5 of the Office Action, certain claims were identified as being indefinite since claim terms/phrases were unclear (35 USC §112, 2nd paragraph). In

particular, the Examiner noted that "capable of converting radiation", "in close proximity", "analyte-specific analyte binding ligand", "the efficiency" and "the intensity" were either unclear or lacked sufficient antecedent basis. Applicant's position regarding each phrase/term is discussed separately below. Reconsideration is respectfully requested.

"capable of converting radiation"

In the context of the application, although one skilled in the art would have no difficulty understanding the phrase "capable of converting radiation", Applicants have amended the pending claims in an attempt to clarify the claims. For example, with respect to the first radiation converting component, claim 1 was amended to recite:

> a first radiation converting component to convert radiation of a first wavelength to radiation having at least one different wavelength by receiving radiation of the first wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the first wavelength, wherein an efficiency of conversion by the first radiation converting component to radiation having at least one wavelength that is different from the first wavelength is dependent on the concentration of the analyte in the housing.

Thus, the first radiation converting components converts radiation of a first wavelength to radiation having at least one wavelength that is different from the first wavelength. The first radiation converting components converts the radiation of the first wavelength by receiving radiation of the first wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the first wavelength. The efficiency of conversion depends on the concentration of analyte in the housing.

Similar amendments were made to claims 13, 29, 71, 74, 75, 78, 102 and 115. Other amendments made to claims 14, 79 and 80 render the rejection moot. As such, it is

believed that the Examiner's concerns regarding "capable of converting radiation" have been addressed by these amendments. Notably, no new matter has been added.

"in close proximity"

The Examiner stated that "in close proximity" is unclear because it is vague as to what distance encompasses a close proximity. In an effort to address the Examiner's concern, claims 8 and 16 were amended.[1] Notably, Applicants have also amended claims 11 and 102 in a manner that is similar to that of claims 8 and 16.

"analyte-specific analyte binding ligand"

Applicants have corrected this inadvertent typographical error. The phrase now recites "analyte-specific binding ligand". No new matter has been added.

"the efficiency" and "the intensity"

Applicants have addressed the Examiner's concern regarding antecedent basis. No new matter has been added.

Rejection of the Claims – 35 USC §§102 and 103

In the Office Action, certain of the claims were rejected as being either anticipated by Chick et al., U.S. Patent 6,040,194 (hereinafter, "Chick"). The remaining claims were rejected as being unpatentable over Chick in view of other U.S. patents. Applicants respectfully disagree. However, in an effort to expedite and simplify the prosecution, Applicants have amended the independent claims to include certain features originally found in a dependent claim (for example, claim 1 has been amended to include certain

[1] The Office Action erroneously stated that claim 3 recited "in close proximity".

features of claim 14, and claim 71 has been amended to include certain features of claim 79).[2] In particular, all of the independent claims have been amended to require:

> a second radiation converting component to convert radiation of a second wavelength to radiation having at least one wavelength that is different from the second wavelength by receiving radiation of the second wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the second wavelength, wherein an efficiency of conversion of the radiation of the second wavelength by the second radiation converting component is independent or substantially independent of the concentration of the analyte in the housing (see, for example, claim 102).

As such, in an effort to present more concise and responsive comments, Applicants focus these remarks on the obviousness rejections pertaining to the features of claims 14 and 79. In this regard, in paragraph 9 of the Office Action, it is stated that claims 14 and 79 are unpatentable over Chick in view of Mathies et al., U.S. Patent 5,654,419, (hereinafter "Mathies"). Applicants respectfully disagree – that is, for at least the reasons set forth below, the amended claims are not unpatentable in view of Chick or Mathies, alone or in combination.

Notably, although this discussion focuses exclusively on amended independent claims 1, 71 and 102, the reasons set forth below are *not* the only reasons the amended independent claims are patentable over Chick, either alone or in combination with Mathies. No inference or conclusion should be drawn that Applicants' response to this rejection is

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[2] Applicants reserve the right to present the same or similar subject matter as described in original claim 1 (or any of the original dependent claims thereof) in this application, at a later date, or in a divisional application.

exhaustive; rather, for the sake of brevity, the remarks focus on some of the patentable aspects of the amended independent claims.

Chick et al., U.S. Patent 6,040,194

Chick describes, among other things, an in vivo FRET ("non-radative fluorescence resonance energy transfer") based sensor for detecting the concentration of an analyte. (See Col., 2, lines 32-35). The sensor, in one embodiment, includes a fluorescence reagent to detect the analyte. (See Col., 2, lines 42-43). The fluorescence reagent emits radiation in response to the excitation by radiation of a particular wavelength. (See Col., 2, lines 47-52). The fluorescence intensity changes in the presence of the analyte being detected. (See Col., 2, lines 56-59).

The reagent may include more than one component. In one embodiment, Chick describes that the reagent includes two components – one being an energy-absorbing donor molecule and the other being an energy-absorbing acceptor molecule. (See Col., 3, lines 9-24).

Chick further describes the basic elements and operation of FRET (see, for example, Col. 7, line 35 to Col. 10, line 55) and a technique to use FRET to measure glucose concentrations (see, for example, Col. 10, lines 59 to Col. 12, line 53). In this regard, Chick describes that the efficiency of conversion of the radiation due to FRET is closely dependent on the concentration of the analyte. (See, for example, Col. 9, lines 21 to Col. 10, line 55). The Chick technique determines the concentration of analyte based solely on the affect the analyte has on the efficiency of conversion of the radiation by the fluorescence reagent. (See, for example, Col. 10, lines 59 to Col. 12, line 53). Indeed,

Chick does not employ a fluorescence reagent whose efficiency of conversion of the radiation is independent or substantially independent of the concentration of the analyte.

Mathies et al., U.S. Patent 5,654,419

Mathies describes, among other things, a variety of fluorophores composed of donor-acceptor pairs which are useful for DNA sequencing experiments. (See, for example, col. 2, lines 11-16 and 59-67). Each Mathies donor-acceptor fluorophore pair is joined by a backbone or chain where the distance between the donor fluorophore and acceptor fluorophore may be varied. (Col. 3, lines 32-34). In this regard, Mathies states that

> [t]o generate the labels, pairs or families of fluorophores are bound to a backbone, particularly a nucleic acid backbone, where one of the members of the families is excited at about the same wavelength. By exploiting the phenomenon of energy transfer, the other members of each of the families emit at detectably different wavelengths. The range of distances between donor and acceptor chromophores is chosen to ensure efficient energy transfer. Furthermore, labels used conjointly are selected to have approximately the same mobility in a separation system. This is achieved by changing the mobility of the labeled entity by varying the distance between the two or more members of the family of fluorophores and choosing labels with the same mobility. (Col. 1, line 65 to Col. 2, line 11).

According to Mathies, the dye pairs may be excited by a single wavelength band and emit at several different wavelengths. (See, for example, Col. 3, lines 5-31). This is accomplished by selecting appropriate donor-acceptor pairs, and spacing therebetween, so that the transfer of energy from one donor to an acceptor results in varying shift (depending on the donor and acceptor) in emitted fluorescence wavelength. (Col. 3, lines 32-43).

In operation, the intensity of emitted fluorescence varies with the concentration of fragments or labels since each fragment/label has some dye attached to it and hence increasing fragment/label concentration reflects an increase in dye concentration. (Col. 4, lines 14-27). However, the efficiency of conversion (from the donor fluorophore to the acceptor fluorophore) does not depend on the concentration of the fragment/label – rather, the efficiency of conversion depends on the spacing or distance between the two fluorophores. Because the two fluorophores are rigidly bound to the backbone (col. 1 lines 65-66, col. 3, lines 32-33), the efficiency of conversion (from the donor fluorophore to the acceptor fluorophore) remains constant.

Thus, although the distance is chosen to ensure efficient energy transfer from the donor dye to the acceptor dye (See, Col. 2, lines 3-5), the efficiency of that conversion remains constant since the fluorophores are bound to the backbone. The Mathies technique further relies upon

> the spacing between the two fluorophores [to] affect the mobility of the label. Therefore, one can use different dye pairs and by varying the distance between the different dye pairs, within a range which still permits good energy transfer, provide for substantially constant mobility for the labels. The mobility is not related to the specific spacing, so that one will empirically determine the effect of the spacing on the mobility of a particular label. However, because of the flexibility in the spacing of the fluorophores in the labels, by synthesizing a few different labels with different spacings and different dye pairs, one can now provide for a family of fluorescent labels, which share a common excitation, that have strong and distinctive emission and a substantially common mobility. (Col. 4, lines 14-27).

Thus, Mathies describes a technique whereby the amount or intensity of fluorescence of donor-acceptor pairs depends on the concentration of the fragments or labels. (Col. 4, lines 14-27). The Mathies technique determines the presence of certain fragments or labels depending on the frequency of the detected radiation. That is, "one will be able to distinguish between the components of the mixture to which different labels have been bound [because] the labels will emit at emission maxima separated by at least 10 nm ...." (Col. 3, lines 15-20). Thus, the Mathies technique relies on fluorophores composed of donor-acceptor pairs that emit light at different emission maxima when excited by a single light source. (See, Col. 3, lines 5-20).

Notably, Mathies does not employ a detection technique based on the efficiency of conversion of the radiation by the fluorescence reagent. Further, Mathies in no way teaches or suggests the use of a fluorescent signal that is independent of the concentration of the fragments or labels. Rather, Mathies is based entirely on the use of donor-acceptor pairs whose intensity depends on the concentration of the fragments or labels.

Claimed Inventions

There are many inventions described in the instant application. In an effort to present a more concise response, the discussion below will focus on only certain aspects or features of the claimed inventions. As mentioned above, this response is not exhaustive; however, for the sake of brevity, these remarks focus on only some of the patentable features of the independent claims.

Amended Independent Claim 1

Amended independent claim 1 describes an analyte sensing device for sensing a concentration of analyte in a fluid, the analyte sensing device comprises a

housing and an analyte sensing component disposed in the housing. The analyte sensing component includes an analyte-specific binding ligand and a macroporous matrix wherein the analyte-specific binding ligand is attached to the surface of, or embedded in the macroporous matrix.

The analyte sensing component also includes a first radiation converting component to convert radiation of a first wavelength to radiation having at least one different wavelength by receiving radiation of the first wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the first wavelength. The efficiency of conversion by the first radiation converting component is dependent on the concentration of the analyte in the housing.

In addition, the analyte sensing component also includes a second radiation converting component to convert radiation of a second wavelength to radiation having at least one wavelength that is different from the second wavelength by receiving radiation of the second wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the second wavelength. The efficiency of conversion of the radiation of the second wavelength by the second radiation converting component is independent or substantially independent of the concentration of the analyte in the housing.

Amended Independent Claim 71

Amended independent claim 71 describes an analyte sensing system including an analyte sensing device, like that set forth in amended claim 1, and (i) a radiation providing unit to provide radiation at the first wavelength and (ii) a radiation detecting unit to detect the radiation of one or more wavelengths including the radiation of

the at least one wavelength that is different from the first and second wavelengths and output data which is representative of the intensity of the radiation of the at least one wavelength emitted by the first and second radiation converting components.

Amended Independent Claim 102

Amended independent claim 102 describes an analyte sensing device for sensing a concentration of analyte in a fluid, the analyte sensing device comprises a housing and an analyte sensing component disposed in the housing. The analyte sensing component includes an analyte-specific binding ligand and a macroporous matrix wherein the analyte-specific binding ligand is attached to the surface of, or embedded in the macroporous matrix.

The analyte sensing component also includes a first radiation converting component to convert radiation of a first wavelength to radiation having at least one different wavelength by receiving radiation of the first wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the first wavelength. The efficiency of conversion by the first radiation converting component is dependent on the concentration of the analyte in the housing.

In addition, the analyte sensing component also includes a second radiation converting component to convert radiation of a second wavelength to radiation having at least one wavelength that is different from the second wavelength by receiving radiation of the second wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the second wavelength. The efficiency of conversion of the radiation of the second wavelength by the second radiation converting component is

independent or substantially independent of the concentration of the analyte in the housing.

The analyte sensing device of amended claim 102 also includes a radiation absorbing component disposed within the housing. The radiation absorbing component includes a proximity to the analyte-specific binding ligand that alters the efficiency of the conversion of the radiation of the first wavelength by the first radiation converting component.

Chick in view of Mathies Does NOT
Render Obvious the Claimed Inventions

Simply put, neither Chick nor Mathies, alone or in combination, teach or suggest (or motivate one skilled in the art to provide) the combination of:

(1) a first radiation converting component to convert radiation of a first wavelength to radiation having at least one different wavelength by receiving radiation of the first wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the first wavelength, wherein the efficiency of conversion by the first radiation converting component is dependent on the concentration of the analyte in the housing; and

(2) a second radiation converting component to convert radiation of a second wavelength to radiation having at least one wavelength that is different from the second wavelength by receiving radiation of the second wavelength and, in response thereto, emitting radiation having at least one wavelength that is different from the second wavelength wherein the efficiency of conversion of the radiation of the second wavelength by the second radiation converting component is

independent or substantially independent of the concentration of the analyte in the housing. (See, for example, amended claim 1).[3]

Although the Chick device and technique includes a fluorescence reagent having an efficiency of conversion of radiation of a first wavelength to another wavelength which is dependent on the concentration of the analyte, Chick neither teaches nor suggests implementing a fluorescence reagent to convert radiation of a second wavelength to at least one wavelength that is different from the second wavelength wherein the efficiency of conversion is independent or substantially independent of the concentration of the analyte in the housing. (See, for example, amended claim 1). That is, Chick describes fluorescence reagents that emit radiation (in response to the excitation by radiation of a particular wavelength) wherein the efficiency of conversion is dependent on the concentration of the analyte being detected. (Chick, Col., 2, lines 47-59, and Col. 9, line 21 to Col. 10, line 57). The detection and analysis techniques of Chick are based solely on the efficiency of conversion of a fluorescence reagent which is dependent on the concentration of the analyte being detected and not independent of the concentration of the analyte being detected.

Chick does not teach or suggest a fluorescence reagent (or the use of such a fluorescence reagent) to emit radiation in response to the excitation by radiation of a particular wavelength wherein the fluorescence intensity is independent (or substantially independent) of the concentration of the analyte being detected. The Chick detection

[3] Notably, the shortcomings of Chick and Mathies, as described in these remarks, are equally applicable to amended independent claims 71 and 102.

technique is based on the affect the analyte has on the efficiency of conversion of the radiation by the fluorescence reagent. (See, Chick, Col. 10, lines 59 to Col. 12, line 53).

Indeed, there is absolutely no suggestion or motivation to one skilled in the art to modify Chick in such a way as to implement fluorescence reagents having an efficiency of conversion (of radiation of a wavelength to radiation of another wavelength) that is independent of the concentration of the analyte being detected. The Chick device and technique is based solely on fluorescence reagent having an efficiency of conversion of radiation of a first wavelength to another wavelength which is dependent on the concentration of the analyte. As such, Chick neither contemplates nor motivates one skilled in the art to include a fluorescence reagent having an efficiency of conversion which is independent of the concentration of the analyte.

Mathies provides no help in this regard. At the outset, it is important to note that the Mathies detection technique is entirely different than the Chick technique. Mathies does not employ a technique based on the efficiency of conversion of the radiation by the fluorescence reagent as does Chick. As mentioned above, in Mathies, the intensity of emitted fluorescence varies with the concentration of fragments or labels since each fragment/label has some dye attached to it and hence increasing fragment/label concentration reflects an increase in dye concentration. (Mathies, Col. 4, lines 14-27). However, the efficiency of conversion (from the donor fluorophore to the acceptor fluorophore) does not depend on the concentration of the fragment/label – rather, the efficiency of conversion depends on the spacing or distance between the fluorophore pair. As such, Mathies does not employ a detection system and technique based on the efficiency of conversion of the radiation by the fluorescence reagent.

In addition, there is absolutely no suggestion or motivation to one skilled in the art to modify Mathies to implement a radiation converting component having an efficiency of conversion (of the radiation of a wavelength to radiation of another wavelength) that is dependent of the concentration of the fragments or labels. Indeed, Mathies *teaches away* from such an approach since the efficiency of conversion (from the donor fluorophore to the acceptor fluorophore) remains constant because the spacing or distance between fluorophore pair is constant. (Mathies, Col. 1 lines 65-66 and Col. 3, lines 32-33). In this regard, Mathies relies solely on the intensity of emitted fluorescence at different frequencies (based on different pairs) which depends on the concentration of fragments or labels since each fragment/label has some dye attached to it and hence increasing fragment/label concentration reflects an increase in dye concentration. (Mathies, Col. 4, lines 14-27). There is no suggestion or motivation to modify the Mathies technique to employ a radiation converting component having an efficiency of conversion that is dependent of the concentration of the fragments or label.

With that in mind, there is no teaching, suggestion or motiviation to combine the Mathies detection technique in or with the Chick detection technique. These techniques are incongruent.

Thus, Mathies simply describes a variety of fluorophores composed of donor-acceptor pairs that emit light at different emission maxima when excited by a single light source. (Mathies, Col. 3, lines 5-20). In this regard, Mathies distinguishes "between the components of the mixture to which different labels have been bound [because] the labels will emit at emission maxima separated by at least 10 nm ...." (Mathies, Col. 3, lines 15-20). Thus, the Mathies technique relies on fluorophores composed of donor-acceptor pairs

that emit light at different emission maxima when excited by a single light source to detect, for example, a particular DNA sequence. (Mathies, Col. 3, lines 43-56).

For each of the fluorophores, however, Mathies describes that the amount or intensity of fluorescence of donor-acceptor pairs depends on the concentration of the fragments or labels. (Col. 4, lines 14-27). There is no teaching in Mathies to employ a system or technique whereby the amount or intensity of fluorescence of a donor-acceptor pair is independent of the concentration of the fragments or labels.

Moreover, there is no suggestion or motivation to one skilled in the art to modify the Mathies system and technique to include a donor-acceptor pair having an intensity of fluorescence that is independent of the concentration of the fragments or labels. In this regard, as noted in the instant application,

> second converting chromophore 26 is selected and/or designed to include a conversion efficiency which is independent (or substantially independent) of the concentration of analyte under investigation. In this way, the change in conversion efficiency, which is dependent on the concentration of analyte, may be more readily deduced by comparing the amount of detected radiation of the first wavelength(s) and the amount of detected radiation of the second wavelength(s). (Page 15, lines 3-8).

As such, even if Chick were modified to include one or more of the Mathies fluorophores bound to the analyte, that combination would still not render the claimed inventions unpatentable. That combination would not, among other things, include:

> (1) a first radiation converting component having an efficiency of conversion of radiation of a first wavelength to radiation of another wavelength which is dependent on the concentration of the analyte in the housing; and

(2) a second radiation converting component having an efficiency of conversion of radiation of a second wavelength to radiation of another wavelength that is independent or substantially independent of the concentration of the analyte in the housing.

In sum, Chick and Mathies, alone or in combination, do not render the claimed inventions obvious.

Dependent Claims

As mentioned above, for the sake of brevity, this response does not present the additional reasons/bases that the dependent claims are patentable over Chick and/or Mathies. Those reasons/bases are numerous. However, for at least the reasons stated above, it is respectfully submitted that the dependent claims are patentable in view of Chick and/or Mathies, either alone or in combination.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and reconsideration of the instant application. Applicants submit that all of the pending claims present patentable subject matter and allowance of the claims is respectfully requested.

It is noted that should a telephone interview expedite the prosecution of this application in any way, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

Date: July 21, 2005

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